

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Xiaobin ZHAO

Appl. No. To be assigned (Cont. of
PCT/GB00/00321)

Filed: August 2, 2001 (PCT File Date: 3
February 2000)

For: **Process For The Production of
Multiple Cross-Linked Hyaluronic
Acid Derivatives**

Art Unit: To be assigned

Examiner: To be assigned

Atty. Docket: 0623.1110001/JMC/TMS

Preliminary Amendment

Commissioner for Patents
Washington, D.C. 20231

Sir:

Before examining the above application, please amend the application as follows.

This Amendment is provided in the following format:

(A) A clean version of each replacement paragraph/section/claim along with
clear instructions for entry;

(B) Starting on a separate page, appropriate remarks and arguments. 37
C.F.R. § 1.111 and MPEP 714; and

(C) Starting on a separate page, a marked-up version entitled: "Version with
markings to show changes made."

It is not believed that extensions of time or fees for net addition of claims are
required beyond those that may otherwise be provided for in documents accompanying this
paper. However, if additional extensions of time are necessary to prevent abandonment of
this application, then such extensions of time are hereby petitioned under 37 C.F.R.

§ 1.136(a), and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 19-0036.

Amendments

In the Specification:

On the first page of the specification, on the line following the title, please insert the following sentence -- This application is a continuation of International Application No. PCT/GB00/00321, filed on 3 February 2000, which was published under PCT Article 21(2) in English and which is fully incorporated herein by reference. --

In the Claims:

Please cancel claims 22 and 23.

Please substitute the following claim 3 for the pending claim 3:

3. (once amended) A process according to claim 1 wherein the crosslinking is effected by means of two or more different bonds selected from the group consisting of ether, ester, sulfone, amine, imino and amide bonds.

Please substitute the following claim 4 for the pending claim 4:

4. (once amended) A process according to claim 1 or claim 2 wherein the crosslinking agent is selected from the group consisting of formaldehyde, gluteraldehyde, divinyl sulfone, a polyanhydride, a polyaldehyde, a polyhydric alcohol, carbodiimide,

epichlorohydrin, ethylene glycol diglycidylether, butanediol diglycidylether, polyglycerol polyglycidylether, polyethylene glycol diglycidylether, polypropylene glycol diglycidylether, and a bis-or poly-epoxy cross-linker.

Please substitute the following claim 5 for the pending claim 5:

5. (once amended) A process according to claim 1 wherein an ether bond is formed using a crosslinking agent selected from the group consisting of bis epoxides and poly epoxides under alkaline conditions.

Please substitute the following claim 6 for the pending claim 6:

6. (once amended) A process according to claim 1 wherein an ester bond is formed using a crosslinking agent selected from the group consisting of bis epoxides and poly epoxides under acidic conditions.

Please substitute the following claim 7 for the pending claim 7:

7. (once amended) A process according to claim 5 wherein the crosslinker is selected from the group consisting of 1,2,3,4-diepoxybutane and 1,2,7,8-diepoxyoctane.

Please substitute the following claim 8 for the pending claim 8:

8. (once amended) A process according to claim 1 wherein an ether bond is formed using a glutaraldehyde cross-linking agent under acidic conditions.

Please substitute the following claim 9 for the pending claim 9:

9. (once amended) A process according to claim 1 wherein the crosslinking of each type of functional group is effected sequentially.

Please substitute the following claim 11 for the pending claim 11:

11. (once amended) A process according to claim 9 wherein HA is first cross-linked via the hydroxyl groups by formation of ether bonds and subsequently cross-linked via the carboxyl groups by formation of ester bonds.

Please substitute the following claim 12 for the pending claim 12:

12. (once amended) A process according to claim 1 wherein the crosslinking of each type of functional group is effected simultaneously.

Please substitute the following claim 13 for the pending claim 13:

13. (once amended) A process according to claim 1 for preparing double crosslinked HA.

Please substitute the following claim 15 for the pending claim 15:

15. (once amended) Multiple cross-linked HA obtainable by a process according to claim 1.

Please substitute the following claim 17 for the pending claim 17:

17. (once amended) Cross-linked HA according to claim 15 wherein the crosslinking bonds are two or more selected from the group consisting of ether, ester, sulfone, amine, imino and amide bonds.

Please substitute the following claim 18 for the pending claim 18:

18. (once amended) Multiple cross-linked HA according to claim 15 in the form of a film.

Please substitute the following claim 19 for the pending claim 19:

19. (once amended) Multiple cross-linked HA according to claim 15 in the form of a gel.

Please substitute the following claim 20 for the pending claim 20:

20. (once amended) HA according to claim 15 which is double cross-linked HA.

Please substitute the following claim 21 for the pending claim 21:

21. (once amended) A product comprising multiple cross-linked HA according to claim 15.

Remarks

Applicants respectfully request that this Preliminary Amendment be entered by the Examiner. By the foregoing amendment, claims 3-9, 11-13, 15 and 17-21 are sought to be amended. Claims 22 and 23 are sought to be canceled. These changes are believed to introduce no new matter, and their entry is respectfully requested.

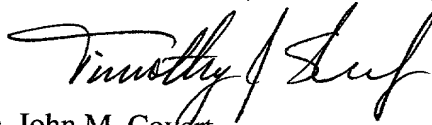
Upon entry of the foregoing amendment, claim 1-21 are pending in the application, with claims 1 and 16 being the independent claims.

Applicants respectfully request that this Preliminary Amendment under 37 C.F.R. § 1.111 be entered by the Examiner. If the Examiner believes that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this application is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.


for John M. Covert
Attorney for Applicant
Registration No. 38,759

Date: August 2, 2001
1100 New York Avenue, N.W.
Suite 600
Washington, D.C. 20005-3934
(202) 371-2600

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Version with markings to show changes made

In the claims:

Please substitute the following claim 3 for the pending claim 3:

3. (once amended) A process according to claim 1 [or claim 2] wherein the crosslinking is effected by means of two or more different bonds selected from the group consisting of ether, ester, sulfone, amine, imino and amide bonds.

Please substitute the following claim 4 for the pending claim 4:

4. (once amended) A process according to [any of claims 1 to 3] claim 1 or claim 2 wherein the cross-linking agent is selected from the group consisting of formaldehyde, gluteraldehyde, divinyl sulfone, a polyanhydride, a polyaldehyde, a polyhydric alcohol, carbodiimide, epichlorohydrin, ethylene glycol diglycidylether, butanediol diglycidylether, polyglycerol polyglycidylether, polyethylene glycol diglycidylether, polypropylene glycol diglycidylether, [or] and a bis-or poly-epoxy cross-linker.

Please substitute the following claim 5 for the pending claim 5:

5. (once amended) A process according to [any of claims] claim 1 [to 4] wherein an ether bond is formed using a crosslinking agent selected from the group consisting of bis epoxides and poly epoxides under alkaline conditions.

Please substitute the following claim 6 for the pending claim 6:

6. (once amended) A process according to [any of claims] claim 1 [to 4] wherein an ester bond is formed using a crosslinking agent selected from the group consisting of bis epoxides and poly epoxides under acidic conditions.

Please substitute the following claim 7 for the pending claim 7:

7. (once amended) A process according to claim 5 [or claim 6] wherein the crosslinker is selected from the group consisting of 1,2,3,4-diepoxybutane and 1,2,7,8-diepoxyoctane.

Please substitute the following claim 8 for the pending claim 8:

8. (once amended) A process according to [any of claims] claim 1 [to 4] wherein an ether bond is formed using a gluteraldehyde cross-linking agent under acidic conditions.

Please substitute the following claim 9 for the pending claim 9:

9. (once amended) A process according to [any of claims] claim 1 [to 8] wherein the crosslinking of each type of functional group is effected sequentially.

Please substitute the following claim 11 for the pending claim 11:

11. (once amended) A process according to claim 9 [or claim 10] wherein HA is first cross-linked via the hydroxyl groups by formation of ether bonds and subsequently cross-linked via the carboxyl groups by formation of ester bonds.

Please substitute the following claim 12 for the pending claim 12:

12. (once amended) A process according to [any of claims] claim 1 [to 8] wherein the crosslinking of each type of functional group is effected simultaneously.

Please substitute the following claim 13 for the pending claim 13:

13. (once amended) A process according to [any of claims] claim 1 [to 12] for preparing double crosslinked HA.

Please substitute the following claim 15 for the pending claim 15:

15. (once amended) Multiple cross-linked HA obtainable by a process according to [any of claims] claim 1 [to 14].

Please substitute the following claim 17 for the pending claim 17:

17. (once amended) Cross-linked HA according to claim 15 [or claim 16] wherein the crosslinking bonds are [selected from] two or more selected from the group consisting of ether, ester, sulfone, amine, imino and amide bonds.

Please substitute the following claim 18 for the pending claim 18:

18. (once amended) Multiple cross-linked HA according to [any of claims] claim 15 [to 17] in the form of a film.

Please substitute the following claim 19 for the pending claim 19:

19. (once amended) Multiple cross-linked HA according to [any of claims] claim 15 [to 17] in the form of a gel.

20. (once amended) HA according to [any of claims] claim 15 [to 19] which is double cross linked HA.

21. (once amended) A product comprising multiple cross-linked HA according to [any of claims] claim 15 [to 20].

Year	Country	Population (millions)	Urban population (millions)	Urban population (%)	Population density (per sq km)	Urban population density (per sq km)
1980	China	959.0	235.0	24.5	120	240
1985	China	1,059.0	275.0	25.9	130	260
1990	China	1,135.0	315.0	27.7	140	280
1995	China	1,210.0	355.0	29.3	150	300
2000	China	1,267.0	395.0	31.2	160	320
2005	China	1,326.0	435.0	32.8	170	340
2010	China	1,385.0	475.0	34.3	180	360
2015	China	1,444.0	515.0	35.7	190	380
2020	China	1,503.0	555.0	37.0	200	400
2025	China	1,562.0	595.0	38.1	210	420
2030	China	1,621.0	635.0	39.2	220	440
2035	China	1,680.0	675.0	40.2	230	460
2040	China	1,739.0	715.0	41.1	240	480
2045	China	1,798.0	755.0	42.0	250	500
2050	China	1,857.0	795.0	42.8	260	520
2055	China	1,916.0	835.0	43.6	270	540
2060	China	1,975.0	875.0	44.3	280	560
2065	China	2,034.0	915.0	45.0	290	580
2070	China	2,093.0	955.0	45.6	300	600
2075	China	2,152.0	995.0	46.2	310	620
2080	China	2,211.0	1,035.0	46.8	320	640
2085	China	2,270.0	1,075.0	47.3	330	660
2090	China	2,329.0	1,115.0	47.9	340	680
2095	China	2,388.0	1,155.0	48.4	350	700
2100	China	2,447.0	1,195.0	48.8	360	720